Amendment to the Claims:

1. (Currently amended) A targeting vector capable of modifying or disrupting a target gene through homologous recombination, said vector comprising:
   a) a first sequence capable of homologously recombining with ~~homologous to~~ a first ~~portion or~~ region of the~~a~~ target gene;
   b) a second sequence capable of homologously recombining with ~~homologous to~~ a second~~portion or~~ region of the~~a~~ target gene;
   c) a selectable marker cassette comprising a DNA sequence encoding a positive selection marker, said cassette located between the first sequence and second sequence; and
   d) a regulator sequence encoding an element capable of repressing expression of the DNA sequence encoding the selection marker; said regulator sequence located adjacent to the first sequence or second sequence, on a side opposite of the selectable marker cassette;

   where homologous recombination of the first sequence and second sequence with the target gene results in expression of the selection marker; and
   where random insertion of the vector into the target gene results in repression of the DNA sequence encoding the selection marker
   ~~, wherein the regulator is located outside the first sequence and second sequence and controls expression of the selectable marker~~;
   ~~wherein the targeting vector is capable of modifying the target gene~~.
2. (Currently amended) The targeting vector of claim 1, wherein the selectable marker cassette further comprises a promoter region ~~and a sequence encoding a selectable marker~~.
3. (Currently amended) The targeting vector of claim 2, wherein the selection~~selectable~~ marker is a marker conferring antibiotic resistance.
4. (Currently amended) The targeting vector of claim 3, wherein the selection~~selectable~~ marker confers resistance to ~~conferring antibiotic resistance is a~~ neomycin ~~resistance gene~~.
5. (Original) The targeting vector of claim 2, wherein the promoter region comprises a promoter sequence.
6. (Original) The targeting vector of claim 5, wherein the promoter sequence is a PGK promoter sequence.

7. (Original) The targeting vector of claim 6, wherein the promoter region further comprises at least one operator sequence.
8. (Previously presented) The targeting vector of claim 7, wherein the operator sequence is a lac operator sequence.
9. (Original) The targeting vector of claim 6, wherein the promoter region comprises the sequence set forth in SEQ ID NO:2.
10. (Currently amended) The targeting vector of claim 1, wherein the element encoded by the regulator sequence is a protein~~inhibits expression of the selectable marker~~.

Claim 11 (Canceled)

12. (Currently amended) The targeting vector of claim ~~1~~10, wherein the protein is a ~~regulator comprises at least one~~ repressor proteinsequence~~.~~
13. (Currently amended) The targeting vector of claim 12, wherein the repressor protein ~~sequence~~ is a lac repressor proteinsequence~~.~~
14. (Currently amended) The targeting vector of claim 13, wherein the element ~~regulator~~ further comprises a nuclear localization signal.
15. (Currently amended) The targeting vector of claim 14, wherein the regulator sequence comprises the sequence set forth in SEQ ID NO:3.
16. (Currently amended) The targeting vector of claim 1, wherein the element encoded by the regulator sequence comprises a transcriptional silencer element.
17. (Currently amended) The targeting vector of claim 14, wherein the sequence encoding the nuclear localization sequence is positioned upstream of the sequence encoding the repressor proteinsequence~~.~~
18. (Currently amended) A method of producing cells comprising a modification of a target gene, the method comprising:

a) introducing into cells capable of homologous recombination a targeting vector of claim 1~~, wherein the targeting vector comprises:~~

i) ~~a first sequence homologous to a portion or region of the target gene;~~

ii) ~~a second sequence homologous to a portion or region of the target gene;~~

iii) ~~a selectable marker cassette located between the first sequence and second sequence; and~~

~~iv) a regulator, wherein the regulator is located outside the first sequence and second sequence and controls expression of the selectable marker~~;

b) selecting for cells expressing the selection~~selectable~~ marker; and

c) identifying cells containing the modification of the target gene.

19. (Original) The method of claim 18, wherein the cells are embryonic stem cells.

20. (Currently amended) A method of identifying cells comprising a disruption or modification of a target gene, the method comprising:

a) introducing into cells capable of homologous recombination a targeting vector of claim 1~~, wherein the targeting vector comprises:~~

~~i) a first sequence homologous to a portion or region of the target gene;~~

~~ii) a second sequence homologous to a portion or region of the target gene;~~

~~iii) a selectable marker cassette located between the first sequence and second sequence; and~~

~~iv) a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker, wherein the selectable marker is positioned within the selectable marker cassette; and wherein the targeting vector is capable of modifying the target gene~~;

b) selecting for cells expressing the selection~~selectable~~ marker; and

c) identifying cells comprising the disruption or modification of the target gene.

21. (Previously presented) The method of claim 20, wherein the cells are embryonic stem cells.

22. (Currently amended) A method of enriching for cells comprising a disruption or modification of a target gene, the method comprising:

a) inserting into cells ~~capble~~ capable of homologous recombination a targeting vector of claim 1~~comprising:~~

i) ~~a first sequence homologous to a portion or region of the target gene;~~

~~ii) a second sequence homologous to a portion or region of the target gene;~~

~~iii) a selectable marker cassette located between the first sequence and second sequence; and~~

~~iv) a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker, wherein the~~

~~selectable marker is positioned within the selectable marker cassette; and wherein the targeting vector is capable of modifying the target gene~~;

b) selecting for cells in which the targeting vector has integrated into the genomes of the cells via homologous recombination, wherein the selected cells express the selection~~selectable~~ marker; and

c) identifying cells containing the disruption or modification of the target gene.

23. (Previously presented) The method of claim 22, wherein the method enhances recovery of cells having the targeting vector integrated via homologous recombination into the genomes of the cells.

24. (Previously presented) The method of claim 22, wherein the cells are embryonic stem cells.

25. (Previously presented) The method of claim 22, wherein the targeting vector is introduced in the cells by electroporation.

26. (Currently amended) An isolated host cell comprising a modification or disruption of a target gene, wherein the target gene is modified or disrupted by insertion of the targeting vector of claim ~~1~~ 32 into the host cell.

27. (Withdrawn) A method of producing a transgenic animal having a genome comprising a modification or disruption of a target gene, the method comprising:

a) introducing a targeting vector into a cell;

b) selecting cells expressing the selectable marker and identifying the cells containing the modification or disruption of the target gene;

c) inserting the cells identified in step (b) into an embryo ; and

d) propogating the transgenic animal from the embryo.

28. (Withdrawn) A transgenic animal comprising a modification or disruption of a target gene within the genome of the transgenic animal, wherein the modification or disruption of the target gene is produced by:

a) introducing a targeting vector into a cell;

b) selecting cells expressing the selectable marker and identifying the cells containing the modification or disruption of the target gene;

c) inserting the cells identified in step (b) into an embryo ; and

d) propogating the transgenic animal from the embryo.

29. (Currently amended) A method of modifying or disrupting the function of a target DNA sequence, the method comprising introducing a targeting vector of claim 1 into a cell, thereby producing a homologous recombinant, wherein the function of the target gene is modified or disrupted~~, and wherein the targeting vector comprises:~~

~~a)a first sequence homologous to a portion or region of the target DNA sequence;~~

~~b)a second sequence homologous to a portion or region the target DNA sequence;~~

~~c)a selectable marker cassette located between the first sequence and second sequence~~; and

~~d)a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker,~~

~~wherein the selectable marker is positioned within the selectable marker cassette~~.

Claims 30, 31 (Canceled)

32. (New) The targeting vector of claim 8, wherein the element encoded by the regulator sequence is a lac repressor protein.